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REVIEW ARTICLE

Dupuytren disease : on our way to a cure ?

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Despite its high prevalence, the clinical presentation and severity of Dupuytren disease is extremely variable. The disease features a broad spectrum of symptoms, from simple nodules without the slightest clinical impact towards an extremely disabling form requiring multiple surgical procedures, sometimes even partial hand amputations. Recurrence after surgery is considered a failure for both patient and surgeon, but its definition is vague. The term 're-contracture' was coined by a patient and reflects the disappointment of recurrent disease. Wether or not a treatment option will insure a definite result, may depend more on the severity of the disease, which is patient specific, than on the treatment method itself. If a patient presents with Dupuytren disease, one should not merely evaluate his hands. Different clinical and personal history features may uncover a severe fibrosis diathesis and both correct information to the patient and an individualized treatment plan are needed. In the near future, a simple genetic test may help to identify patients at risk. Similar to the evolving knowledge and treatment modalities seen in rheumatoid arthritis, treatment of Dupuytren disease is likely to advance in the direction of disease control with pharmacotherapy and single shot minimal invasive enzymatic fasciotomy with collagenase to correct established contractures.

Keywords : Dupuytren disease ; cure ; disease control ; collagenase ; fasciectomy.

INTRODUCTION

Dupuytren disease is highly prevalent in male Caucasians over 50 years of age (*40*). In Flanders, we encounter a 10% prevalence of true contractures, which increases to 30% if milder forms restricted to nodules (Tubiana stage 1) are included (*11*). The disability from Dupuytren disease is not easy to measure with custom disability scores designed for the entire upper limb, but it affects numerous patients sufficiently in daily life to consider surgery (*3,17,26*). The impact on the patient's hand function is related with the limitation of the hand volume (Fig. 1). Numerous surgical techniques have been promoted, but there is scarce scientific evidence to support the superiority of one technique over another. Minimal invasive surgery obviously will allow for a quicker and easier recovery. However, more invasive procedures are often chosen. This may be for technical reasons in severe contractures, or due to the

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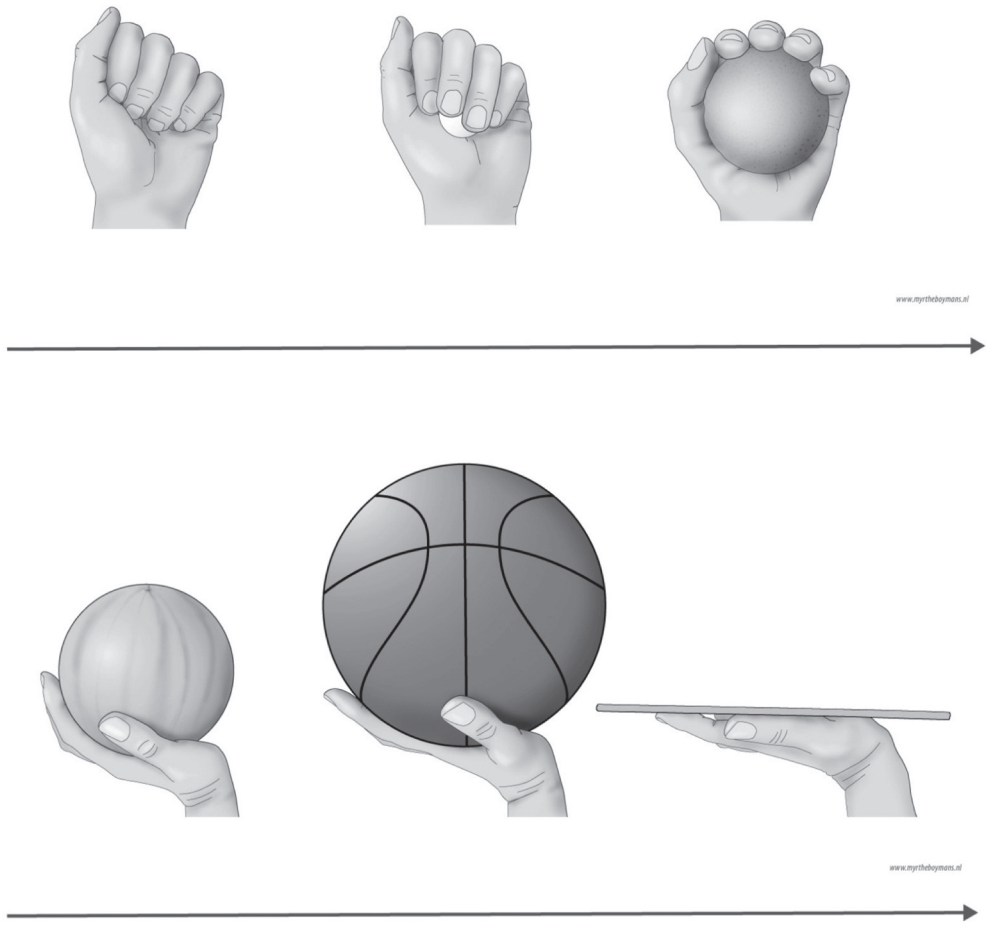

Fig. 1. — The impact on the patient's hand function is related with the limitation of the hand volume, which can be expressed with achievable volumes as illustrated here with balls of different sizes (nothing, a golf ball, tennis ball, melon, basketball and a tablet (full extension)).

surgeon's preference and experience, or to the widespread belief that Dupuytren's nodules need to be entirely removed to prevent 'recurrence' of the disease as if it were a tumour. However, there is increasing evidence that recurrence or extension of Dupuytren disease is more linked to the underlying fibrosis diathesis than it is to surgical technique (*1,9,13*).

SEVERITY OF THE DISEASE

Obviously, more extended contractures of the fingers, with more rays affected, more severe contractures and bilateral affections, will have an increasing impact on the patients' disability in daily life. However, not only does the extensiveness of the disease influence the disability, it is also directly related to Dupuytren's diathesis (*1,10,13*). Patients with a Dupuytren diathesis are more prone to develop severe forms of the disease and are prone to recurrence and extension after surgery. Often, clinical signs not only in the hands, but in other anatomic parts of the human body, can uncover the underlying fibrosis diathesis. Clinical features known to reveal the diathesis are Garrod's knuckle pads, La Peyronie disease and Ledderhose disease. In severe cases, inheritance possibly plays an important role. The genetic background leading to high family occurrence is most likely inherited by means of an autosomal dominant inheritance pattern with

incomplete penetrance (*24*). Other fibroproliferative features may also point to this fibrosis diathesis. For instance Frozen Shoulder syndrome, for instance, appears to be strongly associated with Dupuytren disease (*14,34*).

The severity of Dupuytren disease obviously has a direct impact on the patient's complaints and may influence the technical challenge for the hand surgeon, but it is also likely to influence treatment outcome. More severely affected digits are prone to incomplete surgical correction, with residual extension lack. This is possibly caused by the severity of the contracture, but it is also correlated with a higher fibrosis diathesis, which is reflected by a more pronounced clinical affection of the digits with Dupuytren disease (*13,37*). Multiple-ray contractures are also associated with recurrent disease after surgery.

Precise prediction or classification of Dupuytren disease in terms of severity to formulate an accurate prognosis of individual disease evolution, remains a challenge. At this point, clinical parameters appear to be the only reliable tool to evaluate a patient and to come to a certain view on the severity of the disease. The clinical risk score as defined by Abe is an easy-to-use formula to detect patients at risk (*1*). Up until today, microscopic or immune-histochemical analysis of biopsy tissues have not added to the prognosis of disease evolution (*10*). However, as a genetic background is most likely involved in the inherited and more relentless forms of Dupuytren disease, the future for efficient prognosis and stratification of disease severity may well lie in genetic mapping of patients with Dupuytren disease. Increasing arguments direct to the time-consuming development of a genetic test, which today appears to correlate with clinical features of fibrosis diathesis. In the near future, a reliable genetic test may be available to identify patients at risk for severe Dupuytren disease (*18*). Most naturally, this is not only important to accurately inform the patients about their clinical situation and prognosis, it also is the basis to develop an individualized treatment algorithm. Obviously, alongside genetic mapping of patients, another prerequisite for treatment optimisation is an accurate estimation of the efficiency, risks and benefits of the different treatment modalities.

TREATMENT LADDER

A review of the numerous treatment options in Dupuytren disease easily leads to the conclusion that not one single option will guarantee a definite outcome. To evaluate all treatment methods, one can order them according to their level of invasiveness (Table I). In the truly non-invasive management options, numerous suggestions have been made (*32*). Amongst the most popular proposals are ointment application, mostly with vitamin E, diet changes, splinting, massage and stretching. The efficiency of these various therapeutic measures is supported by no more than case reports. On the next level of invasiveness, one should categorize the so-called non-invasive treatment options, of which the 'innocence' is debatable. Irradiation of stage 1 Dupuytren's nodules has been suggested to prevent disease progression (*4*). However, although surgery may well be feasible in case of disease progression after radiotherapy, the long-term effects of radiotherapy may well outweigh the benefits in this non-malignant condition. Therefore, in Belgium, irradiation of Dupuytren disease is not allowed.

Furthermore, steroid injections and needle fasciotomy are often considered as non-invasive techniques, but are obviously minimal invasive techniques. In needle fasciotomy, the point of the needle is used as a small knife to progressively cut the strands by multiple pricks while putting the finger under traction. This technique has proven its efficiency, with a quick recovery. However, recurrence rates appear to be somewhat higher than in open fasciectomy (*38*). This is probably due to the smaller firebreaks that are created with simple fasciotomy. For these reasons, needle fasciotomy is currently often advised in the elderly patient (*19*). Steroid injections may improve the effect of a needle fasciotomy (*30*).

Next, the firebreak effect can be augmented by choosing minimal invasive techniques or limited surgery. The most popular and innovative treatment method today is the injection of enzymes to dissolve the collagen within the cord that brings about the contracture. Although expensive, with some risk of tendon ruptures and allergic reactions, collagenase injections are currently rapidly gaining popularity,

Table I. — Overview of the numerous treatment modalities in Dupuytren disease, in order of invasiveness with the reported level of evidence on efficiency

Level of invasiveness	Modalities	Scientific evidence
Non-invasive therapy	Ointments, stretching, splinting, diet changes	Case reports Level 4
Arguable non-invasive therapy	Radiotherapy	Outcome studies, no control groups Level 3
Minimal invasive Non-surgical treatment	Needle aponeurotomy Collagenase injections Lipofilling	Outcome studies Therapeutic level 1, economic level 2
Minimal invasive surgery	Segmental resection Cellulose implantation	Outcome studies Randomisation Level 2
Medium invasive surgery	Fasciectomy	Outcome studies Therapeutic level 3
Highly invasive surgery	Subtotal pre-axial amputation (Hueston) Flap surgery	RCTs Case series Level 2
Salvage procedures	Joint arthrodesis Amputation	Case series Level 4

due to their efficiency, to the avoidance of surgery and to the improved medium-term effects as compared to simple needle fasciotomy (*8*). Hovius *et al* have suggested to augment needle fasciotomy with autologous fat injections, and they reported high success rates with this novel technique which originated from a plastic surgery background (*23*).

Alternatively, firebreaks can be enlarged with minimal invasive surgery. Segmental fasciectomy as introduced by Villain and popularized by Moermans, is based on segmental resection of the Dupuytren cords through small curved incisions, which are made in strategically chosen positions (*31*). Next, the cord interruptions can be enhanced with a biologically inert resorbing implant which was developed to prevent scar tissue formation after infertility surgery, neurosurgery and more recently also after tenolysis in hand surgery. Cellulose implants not only appear to improve the contractures and satisfaction after surgery, furthermore the skin is separated from the underlying fibroproliferative tissue which adds to the early mobilization after surgery (*15*).

Full resection of the cords is the next level of surgery. Here, surgical procedures may be limited to fasciectomy of a single strand with different approaches. A clue to a good approach is to avoid scar retraction with concurrent finger re-contracture. Therefore, longitudinal incisions need to be avoided in each case, certainly over the joints. A Bruner zigzag incision is the most commonly used approach and in skin shortage often a Z-plasty is preferred (*6,35*). However, if skin shortage cannot be addressed with a Z-plasty, open techniques inspired by the historical 'open palm' of McCash will require long term wound care to achieve secondary healing (*29*). To avoid this long standing open wound and also to increase the firebreak effect, Hueston introduced the full thickness grafting (*25,36*). In case severe skin and subcutaneous defects are unavoidable to surgically address important contractures, local or free flaps may be considered.

However, surgery in Dupuytren disease implies a significant complication risk (*7*). This risk is increased if multiple surgical procedures are repeated in recurrent disease. Injury of nerves or blood vessels may lead to painful retracted fingers and amputation surgery may then have to be considered. In fact, Dupuytren disease is the most important reason for elective finger amputation in hand surgery and is done in almost every case after 'failed' earlier surgical procedures (*12*). Other salvage procedures may be chosen for cosmetic (and often functional) reasons e.g. limited finger arthrodesis (*33*).

An alternative to address long standing finger contractures could be the application of a progressive extension torque with the help of an external device with springs or screws, but such a device is not yet available in Europe (*2*).

Which surgical procedure do surgeon and patient need to choose within this extensive option menu ? Up until today, no outcome studies can absolutely sustain the superiority of one method over another (*5*) (Table I). This is due to the lack of standardization of the intended to treat population, the absence of randomization and the need for clear definitions as for example for recurrence. The choice of a surgical technique is dependent of technical issues and to the author's opinion, it is necessary to at least have experience in all surgical options. If not, the metaphor of everything resembling a nail if one only possesses a hammer, may risk to apply. The choice of a surgical technique needs to be individualized according to the severity of the disease, the severity of the contractures, the involvement of the skin and joints and the wishes of the patient. Further randomized outcome studies in similar (high risk) patients, may clarify the efficiency of the different surgical techniques after a thorough analysis of the risks and benefits. However, more drastic surgery may interfere with subsequent rehabilitation, without a guarantee with respect to the results (*9*). The surgeon needs to bear in mind that he can cut out strands, but not the disease itself. Therefore, minimal invasive techniques should be considered whenever feasible and further research for disease control is mandatory (Fig. 2).

DISEASE CONTROL

Dupuytren disease is an intriguing pathology to numerous hand surgeons and basic scientist. Along with the research on other fibroproliferative processes like scar tissue formation, burns and desmoid

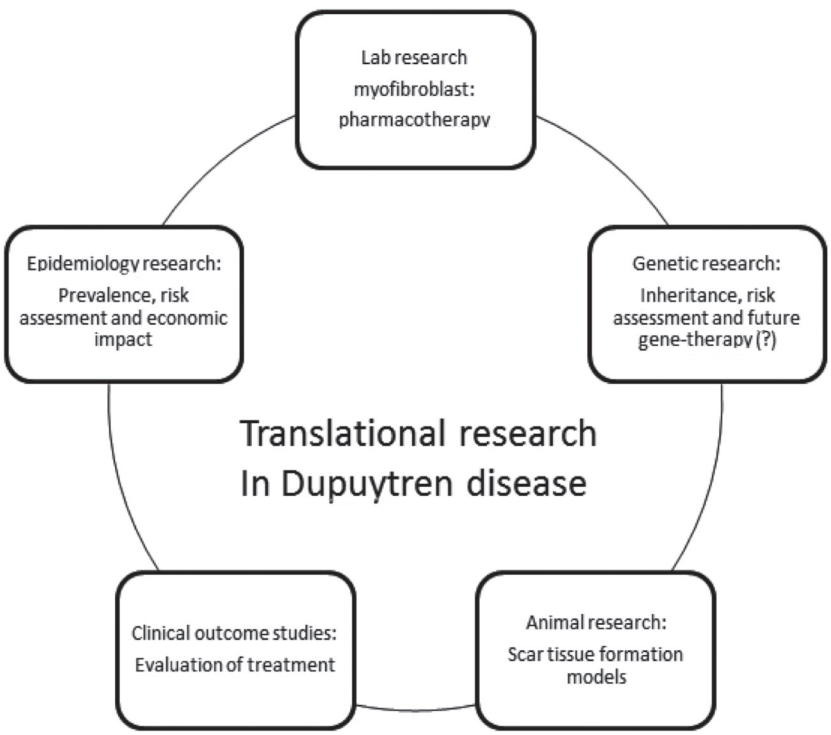

Fig. 2. — The diagram illustrates the impact and importance of the translational research in all its facets, needed to optimize the treatment of Dupuytren disease. Scientific theories resulting from basic research need to be tested in clinical practice, with practical applications like pharmacotherapy. On its turn, clinical research will lead to the evocation of new scientific questions that need to be answered by further basic research guided by the continuous clinical challenges.

tumours, knowledge of the underlying cellular pathways in Dupuytren's disease is increasing every year.

The debate on whether Dupuytren's disease is a process more resembling a tumour growth or an inflammatory disease is not yet be completely resolved. However, arguments for the latter are increasing rapidly. Wang *et al* have suggested that palmar fibromatosis is a reactive proliferation rather than a neoplasm, based on clonal analysis of the tissue (*39*). The similarities with an inflammatory process inspires to a future disease control, rather than a primary and profound resection of all affected tissue. Possibly, both surgery and pharmacotherapy may be combined, with an improved outcome in risk patients. Preliminary results of a placebo-controlled randomized controlled trial with highly dosed neo-adjuvant tamoxifen in segmental fasciectomy, demonstrated superior short term outcome (*16*).

Similar studies with other agents are currently conducted and are the result of translational research, wherein laboratory findings are directly translated into clinical research.

WHAT WILL THE FUTURE BRING ?

With the current trends, surgery may one day be replaced by minimal invasive therapy and manipulation techniques as is currently being introduced with enzymatic fasciotomy . In case of pending recurrence, pharmacotherapy may prevent further disease evolution. Expectantly in the near future, severe Dupuytren's disease patients will receive disease control treatment, perhaps even without surgical intervention. With the impending developments of genetic screening, recurrence may be treated early, even before the first signs are present.

CONCLUSION

Current evolution in the understanding of Dupuytren's disease is giving rise to a treatment algorithm shift. The long-standing epoch of standard surgical strand removal, nowadays has evolved to a broad spectrum of treatment options. This urges the need for treatment algorithms. First, a patient with Dupuytren disease needs to be identified properly with a thorough assessment of his fibrosis diathesis. At this point, fibrosis diathesis can be estimated with clinical parameters, but in the near future it may well be done by a genetic screening test. Next, minimal invasive treatment options should be considered for the sole purpose of damage control and the current trend of enzymatic fasciotomy is promising. Finally, disease control with pharmacotherapy may well prevent recurrence in patients at risk in the near future and translational research is required for the further development of efficient disease control.

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